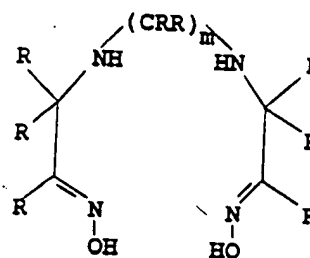


What is claimed is:

1. A compound of the formulae

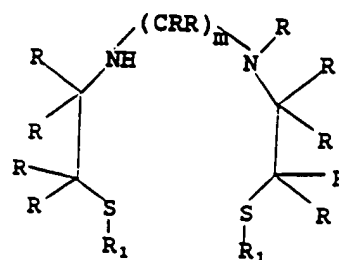
5 Ia

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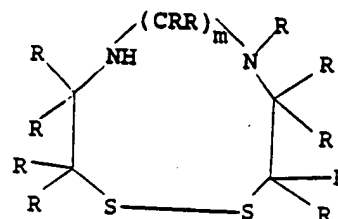
15 Ib

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25 Ic

30



where at least one R is $-(A)_p-R_2$ where $(A)_p$ is a linking group and R_2 is a hypoxia localizing moiety; and wherein the other R groups are the same, or different and are independently selected

from hydrogen, halogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, aryl, $-\text{COOR}_3$, $-\overset{\text{O}}{\parallel}\text{C}-\text{NHR}_3$, $-\text{NH}_2$, hydroxyalkyl, alkoxyalkyl, hydroxyaryl, haloalkyl, arylalkyl, $-\text{alkyl}-\text{COOR}_3$, $-\text{alkyl}-\text{CON}(\text{R}_3)_2$, $-\text{alkyl}-\text{N}(\text{R}_3)_2$, $-\text{aryl}-\text{COOR}_3$, $-\text{aryl}-\text{CON}(\text{R}_3)_2$, $-\text{aryl}-\text{N}(\text{R}_3)_2$, 5- or 6-membered nitrogen- or oxygen-containing heterocycle; or two R groups taken together with the one or more atoms to which they are attached form a carbocyclic or heterocyclic, saturated or unsaturated spiro or fused ring which may be substituted with R groups;

R_1 is hydrogen, a thiol protecting group or $-(\text{A})_p-\text{R}_2$;

R_3 is hydrogen, alkyl or aryl;
 $m = 2$ to 5 ;
 $p = 0$ to 20 .

2. A complex of a metal and a ligand, which ligand includes a hypoxia-localizing moiety, wherein said complex has a permeability through cell membranes greater than that of ^{14}C -sucrose.

3. The complex of claim 2 having a coordination number less than 7.

4. The complex of claim 2 wherein the metal is non-radioactive.

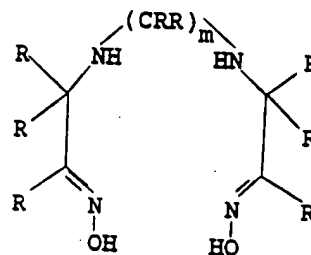
5. The complex of claim 2 wherein the metal is radioactive.

6. The complex of claim 5 wherein said metal is technetium or rhenium.

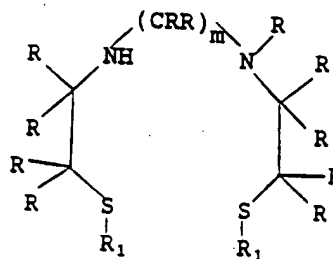
7. The complex of claim 6 wherein said metal is in the +5 oxidation state.

8. The complex of claim 2 wherein said ligand forms a chelate with said metal.
9. The complex of claim 8 wherein said complex is formed from a bidentate ligand.
10. The complex of claim 8 wherein said complex is formed from a tridentate ligand.
11. The complex of claim 8 wherein said complex is formed from a tetradentate ligand.
12. The complex of claim 2 wherein said ligand is selected from

Ia



Ib



where at least one R is $-(A)_p-R_2$ where $(A)_p$ is a linking group and R_2 is a hypoxia localizing moiety; and wherein the other R groups are the same, or different and are independently selected

from hydrogen, halogen, hydroxy, alkyl, alkenyl,

alkynyl, alkoxy, aryl, $-\text{COOR}_3$, $-\overset{\text{O}}{\underset{\parallel}{\text{C}}}-\text{NHR}_3$, $-\text{NH}_2$,
hydroxyalkyl, alkoxyalkyl, hydroxyaryl, haloalkyl,

5 arylalkyl, $-\text{alkyl}-\text{COOR}_3$, $-\text{alkyl}-\text{CON}(\text{R}_3)_2$,
 $-\text{alkyl}-\text{N}(\text{R}_3)_2$, $-\text{aryl}-\text{COOR}_3$, $-\text{aryl}-\text{CON}(\text{R}_3)_2$,
 $-\text{aryl}-\text{N}(\text{R}_3)_2$, 5- or 6-membered nitrogen- or oxygen-
containing heterocycle; or two R groups taken
together with the one or more atoms to which they
10 are attached form a carbocyclic or heterocyclic,
saturated or unsaturated spiro or fused ring which
may be substituted with R groups;

R_3 is hydrogen, alkyl or aryl;

$m = 2$ to 5 ;

15 $p = 0$ to 20 .

13. The complex of claim 12, wherein said ligand is
selected from formula Ia or Ib, and where the metal is a
radionuclide of technetium.

14. The complex of claim 12, wherein said ligand
has the formula Ib, and wherein said metal is a
20 radionuclide of rhenium.

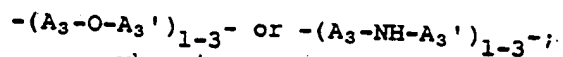
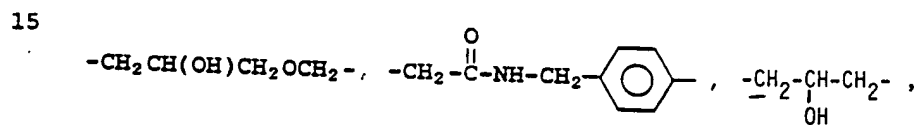
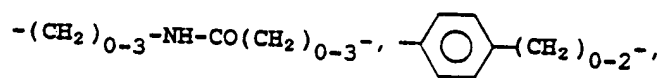
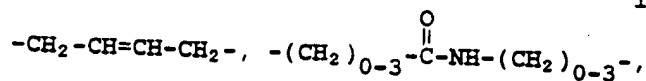
15. The metal complex of claim 12 containing
the linking group $(\text{A})_p$, wherein p is an integer
greater than zero, and the various A units (which
form a straight or branched chain) are independently
25 selected from $-\text{CH}_2-$, $-\text{CHR}_4-$, $-\text{CR}_4\text{R}_5-$, $-\text{CH}=\text{CH}-$,
 $-\text{CH}=\text{CR}_4-$, $-\text{CR}_4=\text{CR}_5-$, $-\text{C}\equiv\text{C}-$, cycloalkyl, cyclo-
alkenyl, aryl, heterocyclo,

oxygen, sulfur, $-\overset{\text{O}}{\underset{\parallel}{\text{C}}}-$, $-\text{NH}-$, $-\text{HC}=\text{N}-$, $-\text{CR}_4=\text{N}-$,
30 $-\text{NR}_4-$, $-\text{CS}-$; wherein R_4 and R_5 are independently
selected from alkyl, alkenyl, alkoxy, aryl, 5- or

6-membered nitrogen- or oxygen-containing hetero-cycle, halogen, hydroxy or hydroxyalkyl.

16. The metal complex of claim 15 wherein (A)_p is absent or is selected from alkyl, oxa-alkyl, hydroxyalkyl, hydroxyalkoxy, alkenyl arylalkyl, alkenyl, arylalkylamide, alkylamide, alkylamine and (alkylamine)alkyl.

17. The metal complex of claim 16 wherein (A)_p is absent or is selected from -(CH₂)₁₋₅-,

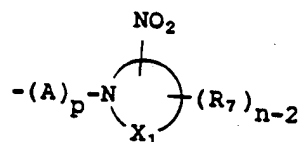


20 wherein A₃ and A₃' are the same or different alkyl.

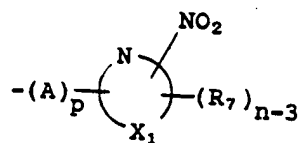
18. A metal complex in accordance with claim 12 wherein the hypoxia localizing moiety (R₂) is a hypoxia-mediated nitro-heterocyclic group.

19. A complex in accordance with claim 18 wherein said linker/hypoxia-localizing portion of the complex are selected from

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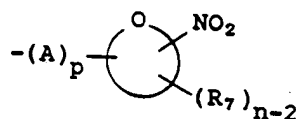
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or

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the ring portion being a 5- or 6-membered cyclic or aromatic ring, wherein;

n is the total number of substitution positions available on the 5- or 6-membered ring;

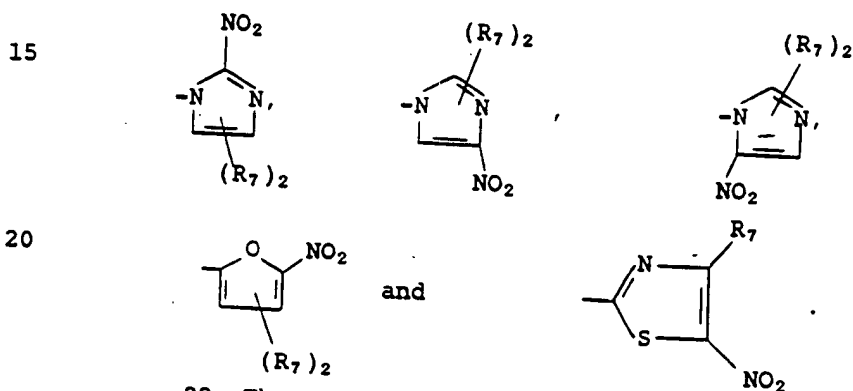
one or more of said R₇ groups are independently hydrogen, halogen, alkyl, aryl, alkoxy, hydroxy, hydroxyalkyl, hydroxyalkoxy, alkenyl, arylalkyl, arylalkylamide, alkylamide, alkylamine and (alkylamine)alkyl;

X₁ is nitrogen, sulfur, oxygen, -CR₇= or -CRR-; and

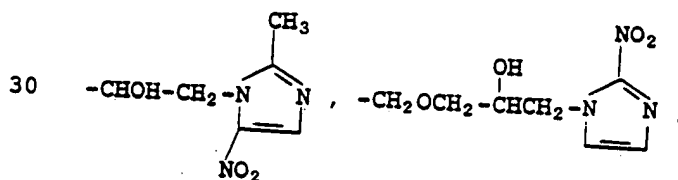
(A)_p can be absent in which case the nitro-heterocyclic hypoxia localizing moiety is linked to the rest of the complex of claim 18 via a ring nitrogen or carbon atom, or (A)_p comprises the link
 5 between the nitro-heterocyclic group and said rest of the complex of claim 18.

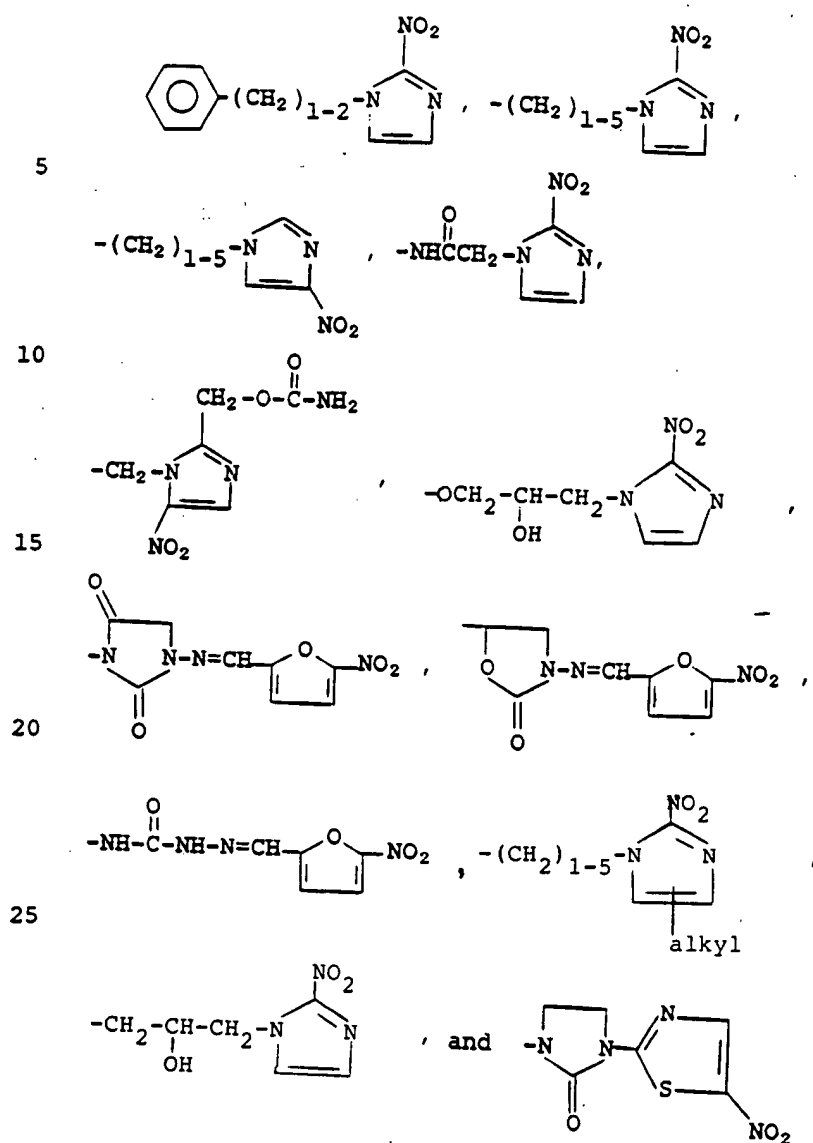
20. The complex of claim 18 wherein said hypoxia-mediated nitro-heterocyclic group is selected from 2-, 4- or 5-nitroimidazoles, nitro-furans, nitrothiazoles and derivatives thereof.
 10

21. The complex of claim 20 wherein said localizing group of the complex is selected from

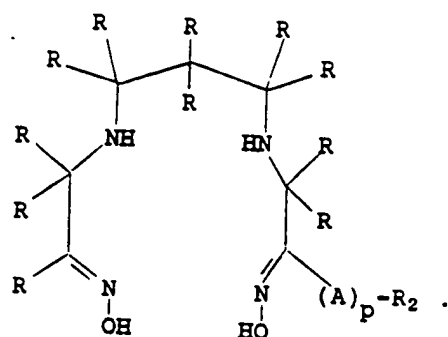


22. The complex of claim 20 wherein the
 25 linking group/localizing moiety portion of the complex is selected from



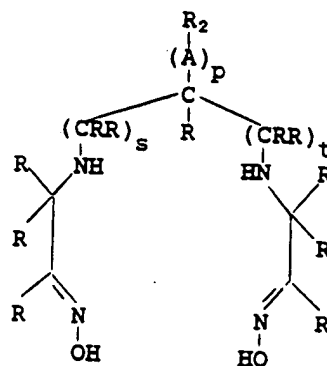


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26. The complex of claim 25 wherein R₂ is a nitroheterocyclic group and each R can be hydrogen or alkyl.

27. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

28. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-1-(4-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

29. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 4,4,10,10-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-5,9-diazadodecane-3,11-dione dioxime.

30. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 6-hydroxy-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

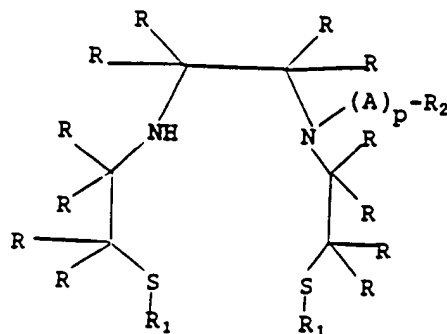
31. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-6-((2-nitro-1H-imidazol-1-yl)acetamido)-4,8-diazaundecane-2,10-dione dioxime.

32. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-6-((2-nitro-1H-imidazol-1-yl)ethyl)-4,8-diazaundecane-2,10-dione dioxime.

33. The complex of claim 12 wherein the ligand is of the formula

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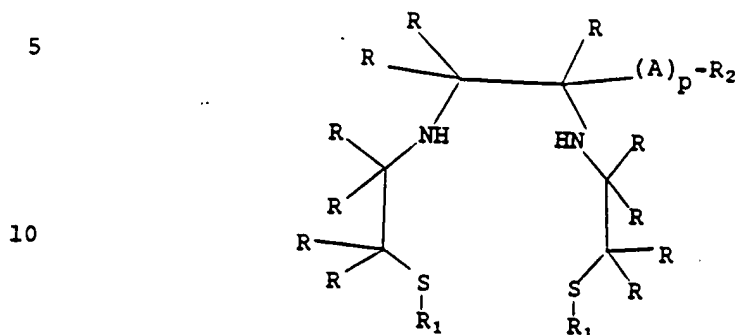
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20 wherein R_1 is selected from H or a thiol protecting group and the other R groups are independently selected from H, hydroxy or alkyl.

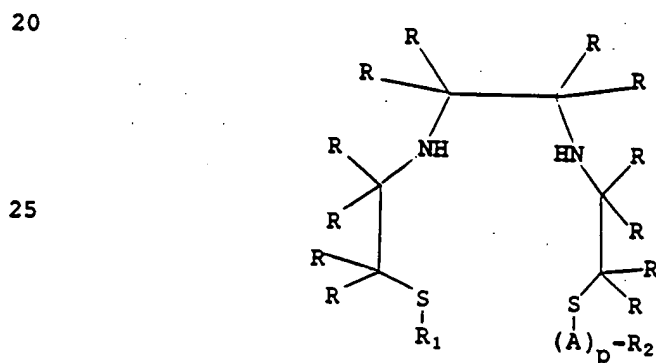
34. A complex of claim 33 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety wherein said ligand has the name 5,8-diaza-1,2-dithia-5-(2-(2-nitro-1H-imidazol-1-yl)-ethyl)-3,3,10,10-tetramethylcyclodecane.

35. The complex of claim 12 wherein the ligand is of the formula



15 wherein R_1 is selected from H or a thiol protecting group and the other R groups are independently selected from H, hydroxy or alkyl.

36. The complex of claim 12 wherein the ligand is of the formula



30 wherein R_1 is selected from H or a thiol protecting group and the other R groups are independently selected from H, hydroxy or alkyl or two R groups taken together with the one or more atoms to which they are attached form a carbocyclic or heterocyclic saturated or unsaturated spiro or fused ring which may be substituted with R groups.

35

37. A kit suitable for preparation of a metal complex of claim 2 comprising a source of a ligand selected from the compounds of claim 1; and a reducing agent.

38. The kit of claim 37 wherein said reducing agent is a stannous compound.

39. The kit of claim 37 wherein said metal is selected from technetium and rhenium.

40. A multivial kit suitable for preparation of a metal complex of claim 2 comprising in a first vial

a source of an exchange ligand; and a reducing agent; and,

in a second vial, a source of a ligand selected from the compounds of claim 1.

41. The kit of claim 40 wherein said reducing agent is a stannous compound.

42. The kit of claim 40 wherein said exchange ligand is selected from glucoheptonate, diethylenetriamine pentaacetic acid, mannitol, malate, citric acid and tartaric acid.

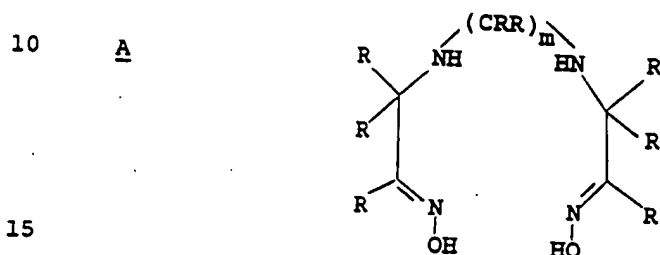
43. The kit of claim 40 wherein said metal is selected from technetium and rhenium.

44. A process for preparing an alkylene diamineoxime comprising reacting an alkylene diamine with two equivalents of a haloketone to provide an alkylene diaminediketone which is thereafter converted to said alkylene diaminedioxime; or

reacting an alkylene diamine with one equivalent of a first haloketone and reacting the resulting product with one equivalent of a second haloketone and thereafter converting to said alkylene diaminedioxime; or

reacting an alkylene diamine with one equivalent of a chloronitroso, then reacting the product with a haloketone, thereafter converting to said alkylene diamine dioxime.

45. A process for preparing a compound of the formula



where at least one R is $-(A)_p-R_2$ where $(A)_p$ is a linking group and R_2 is a hypoxia localizing moiety; and wherein the other R groups are the same, or different and are independently selected from hydrogen, halogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, aryl, $-COOR_3$, $-\overset{\overset{O}{\parallel}}{C}-NHR_3$, $-NH_2$, hydroxyalkyl, alkoxyalkyl, hydroxyaryl, haloalkyl, arylalkyl, $-alkyl-COOR_3$, $-alkyl-CON(R_3)_2$, $-alkyl-N(R_3)_2$, $-aryl-COOR_3$, $-aryl-CON(R_3)_2$, $-aryl-N(R_3)_2$, 5- or 6-membered nitrogen- or oxygen-containing heterocycle; or two R groups taken together with the one or more atoms to which they are attached form a carbocyclic or heterocyclic, saturated, unsaturated or aromatic spiro or fused ring which may be substituted with R groups;

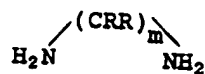
R_3 is hydrogen, alkyl or aryl;

$m = 2$ to 5 ; and,

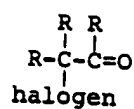
$p = 0$ to 20 ;

which process comprises

5 reacting a compound of the formula



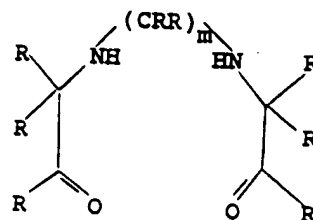
10 with two equivalents of a haloketone of the formula



15

to provide a diketone of the formula

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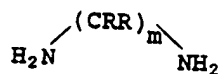


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which is thereafter converted to the corresponding dioxime products;

reacting a compound of the formula

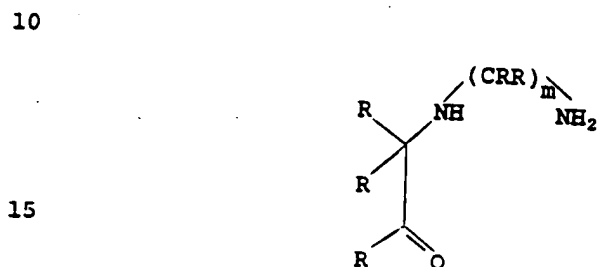
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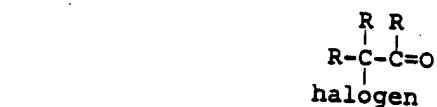
with one equivalent of a first haloketone of the formula



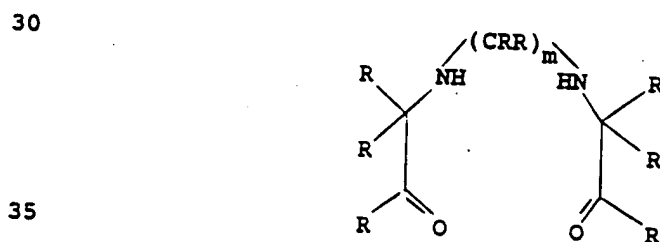
to provide an intermediate of the formula



which is thereafter reacted with one equivalent of a second haloketone of the formula

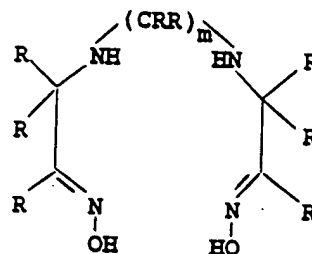


25 wherein at least one of the R groups on said second haloketone differs from the corresponding R groups on said first haloketone, to provide an intermediate of the formula



and thereafter converting to the corresponding dioxime wherein the R groups substituting said first amine oxime portion of the compound of formula A differ from the R groups substituting said second amine oxime portion.

46. A process for preparing a compound of the formula



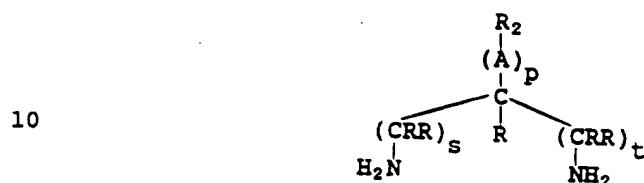
where at least one R is $-(A)_p-R_2$ where $(A)_p$ is a linking group and R_2 is a hypoxia localizing moiety; and wherein the other R groups are the same, or different and are independently selected from hydrogen, halogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, aryl, $-\text{COOR}_3$, $-\overset{\text{O}}{\parallel}\text{C}-\text{NHR}_3$, $-\text{NH}_2$, hydroxyalkyl, alkoxyalkyl, hydroxyaryl, haloalkyl, arylalkyl, $-\text{alkyl}-\text{COOR}_3$, $-\text{alkyl}-\text{CON}(\text{R}_3)_2$, $-\text{alkyl}-\text{N}(\text{R}_3)_2$, $-\text{aryl}-\text{COOR}_3$, $-\text{aryl}-\text{CON}(\text{R}_3)_2$, $-\text{aryl}-\text{N}(\text{R}_3)_2$, 5- or 6-membered nitrogen- or oxygen-containing heterocycle; or two R groups taken together with the one or more atoms to which they are attached form a carbocyclic or heterocyclic, saturated, unsaturated or aromatic spiro or fused ring which may be substituted with R groups;

$m = 2$ to 5; and,

p = 0 to 20;

which process comprises:

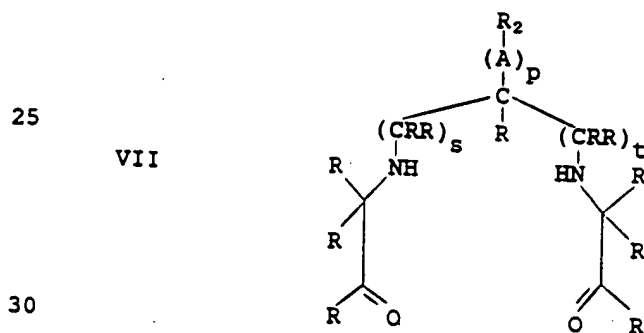
a) reacting a compound of the formula



where s is 0 to 4 and t is 0 to 4 with the proviso that $s + t$ is not greater than 4 with two equivalents of a compound the formula

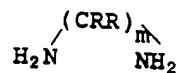


where halogen is Br, Cl or I, to provide a diketone of the formula .

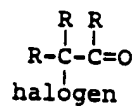


and thereafter converting the diketone to the corresponding dioxime; or

b) reacting a compound of the formula



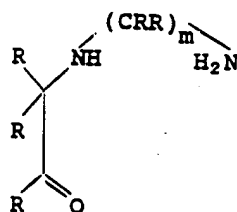
5 with one equivalent of a first compound of the formula



10 to provide a compound of the formula

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VIII

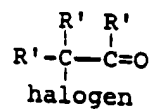


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and thereafter reacting with a compound of the formula

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VI'

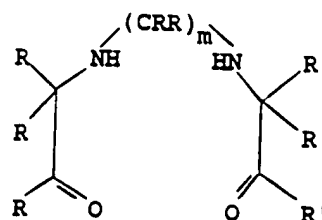


30 where R' = R but where one of the R' groups must be $-(A)_p-R_2$

to provide the diketone

IX

5



10 (where one of the R' must be $-(A)_p-R_2$)

which is thereafter converted to the corresponding dioxime.

15 47. A method for the diagnostic imaging of hypoxic tissue in a mammalian species comprising the administration of a metal complex of the ligands of formula Ia or Ib in claim 12 wherein the metal is a radionuclide of technetium and the hypoxia-localizing moiety is or contains a hypoxia-mediated nitro-heterocyclic group.

20 48. The method of claim 47 used to diagnose ischemic tissue in the heart.

49. The method of claim 47 used to diagnose ischemic tissue in the lung.

25 50. The method of claim 47 used to diagnose ischemic tissue in the kidneys or liver.

51. The method of claim 47 used to diagnose ischemic tissue in the brain.

30 52. The method of claim 47 used to diagnose hypoxic tissue in tumors.

53. A method for providing radiotherapy to a mammalian species in need thereof comprising the administration of a complex of formula Ia or Ib in claim 12 wherein the metal is a radionuclide of rhenium and wherein the hypoxia localizing moiety is or contains a hypoxia-mediated nitro-hetero-cyclic group.

54. A method for perfusion imaging of blood flow in a mammalian species comprising the administration of a metal complex of the ligands of formula Ia or Ib in claim 12 wherein the metal is a radionuclide of technetium.

55. A compound of claim 1 having the name 3,3,6,6,9,9-hexamethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

56. A compound of claim 1 having the name 6,6-diethyl-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

57. A compound of claim 1 having the name 6,6-diethyl-3,3,9,9-tetramethyl-1-(4-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

58. A compound of claim 1 having the name 3,3,9,9-tetramethyl-1,11-bis(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

59. A compound of claim 1 having the name 3,3,9,9-tetramethyl-6-methoxy-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

60. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name [⁹⁹Tc] oxo[[4,4,10,10-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-5,9-diazadodecane-3,11-dione dioximato] (3-)-N,N',N'',N'''] technetium(V).

61. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name [^{99m}Tc] oxo[[3,3,6,6,9,9-hexamethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioximato] (3-)-N,N',N'',N''']technetium(V).

62. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name [^{99m}Tc] oxo[[3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioximato] (3-)-N,N',N'',N''']technetium(V).

63. A compound of claim 1 having the name 3,3,6,9,9-pentamethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

64. A compound of claim 1 having the name 12-methoxycarbonyl-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

65. A compound of claim 1 having the name 11-ethoxy-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

66. A compound of claim 1 having the name 3,3,9,9-tetramethyl-6-[2-hydroxy-3-(2-nitro-

1H-imidazol-1-yl)propyl]-4,8-diazaundecane-2,10-dione dioxime.

67. A compound of claim 1 having the name 3,3,9,9-tetramethyl-1-(4-methyl-2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

68. A compound of claim 1 having the name 3,3,9,9-tetramethyl-1-(5-methyl-2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

69. A compound of claim 1 having the name 6,6-difluoro-3,3,9,9-tetramethyl-12-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

70. A compound of claim 1 having the name 3,3,9,9-tetramethyl-1-[2-hydroxy-3-(2-nitro-1H-imidazol-1-yl)propoxy]-4,8-diazaundecane-2,10-dione dioxime.

71. A compound of claim 1 having the name 6-hydroxy-3,3,9,9-tetramethyl-12-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

72. A compound of claim 1 having the name 4,4,10,10-tetramethyl-1,13-bis(2-nitro-1H-imidazol-1-yl)-5,9-diazatridecane-3,11-dione dioxime.

73. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,6,9,9-pentamethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

74. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-

localizing moiety, wherein said ligand/localizing moiety has the name 12-methoxycarbonyl-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

5 75. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 11-ethoxy-3,3,9,9-tetramethyl-1-(2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-
10 2,10-dione dioxime.

 76. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-6-[2-
15 hydroxy-3-(2-nitro-1H-imidazol-1-yl)propyl]-4,8-diazaundecane-2,10-dione dioxime.

 77. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing
20 moiety has the name 3,3,9,9-tetramethyl-1-(4-methyl-2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

 78. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-
25 localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-1-(5-methyl-2-nitro-1H-imidazol-1-yl)-4,8-diazaundecane-2,10-dione dioxime.

 79. A complex of claim 2 comprising a
30 radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 6,6-difluoro-3,3,9,9-tetramethyl-12-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

80. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 3,3,9,9-tetramethyl-1-

5 [2-hydroxy-3-(2-nitro-1H-imidazol-1-yl)propoxy]-4,8-diazaundecane-2,10-dione dioxime.

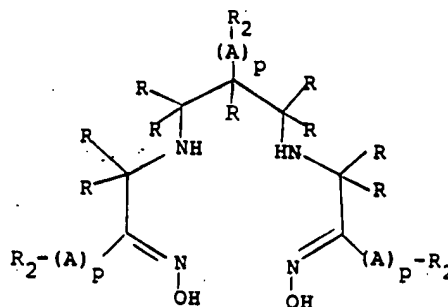
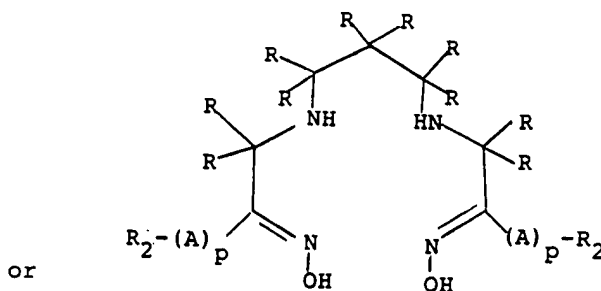
81. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-localizing moiety, wherein said ligand/localizing moiety has the name 6-hydroxy-3,3,9,9-

10 tetramethyl-12-(2-nitro-1H-imidazol-1-yl)-4,8-diazadodecane-2,10-dione dioxime.

82. A complex of claim 2 comprising a radionuclide and a ligand bound to a hypoxia-

15 localizing moiety, wherein said ligand/localizing moiety has the name 4,4,10,10-tetramethyl-1,13-bis(2-nitro-1H-imidazol-1-yl)-5,9-diazatri-decane-3,11-dione dioxime.

83. A compound of claim 1 which is



84. A multivial kit suitable for
preparation of a metal complex of claim 2
comprising

in a first vial a source of reducing agent,
5 and
in a second vial a source of a ligand
selected from the compounds of claim 1.